

Amendments to the Claims:

1-2 (canceled)

3. (new) A method of detecting binding of a PAS (Per-ARNT-Sim) domain of a protein with a foreign core ligand of the PAS domain, wherein the PAS domain is prefolded in its native state, the method comprising the steps of:

determining from NMR analysis of the PAS domain that the PAS domain comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity;

detecting a first NMR spectrum of the PAS domain in the presence of a foreign ligand;

comparing the first NMR spectrum with a second NMR spectrum of the PAS domain in the absence of the ligand; and

determining the presence of the ligand specifically bound within the hydrophobic core of the PAS domain.

4. (new) The method of claim 3, wherein the PAS domain is the PAS A domain of PAS kinase.

5. (new) The method of claim 3 wherein the protein consists of the PAS domain.

6. (new) The method of claim 3, wherein the foreign ligand is a small organic compound.